PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference PCT-7819	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IT 03/00757	International filing date *(day/month/year)* 20.11.2003	Priority date *(day/month/year)* 13.12.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/21		
Applicant SIGMA-TAU INDUSTRIE FARMACEUTICHE RIUNITE S.P.A.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
16.06.2004	08.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Albayrak, T Telephone No. +49 89 2399-7549

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IT 03/00757

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-31 as originally filed

Claims, Numbers

1-9 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-9
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	-

2. Citations and explanations

see separate sheet

Re Item I

The basis of this written opinion is the application as originally filed.

Re Item V

1. Reference is made to the following documents; unless otherwise indicated, reference is made to the relevant passages emphasized in the Search Report.

   D1: EP-A-0 681 839 (KURATSUNE HIROHIKO ;KITANI TERUO (JP)) 15 November 1995 (1995-11-15)
   D2: US-A-6 037 373 (DE SIMONE CLAUDIO) 14 March 2000 (2000-03-14)
   D3: CAVALLINI G ET AL: "ORAL PROPIONYL-L-CARNITINE AND INTRAPLAQUE VERAPAMIL IN THE THERAPY OF ADVANCED AND RESISTANT PEYRONIE'S DISEASE" BJU INTERNATIONAL, BLACKWELL SCIENCE, OXFORD, GB, vol. 89, no. 9, June 2002 (2002-06), pages 895-900, XP001146228 ISSN: 1464-4096
   D4: BIAGIOTTI G ET AL: "ACETYL-L-CARNITINE VS TAMOXIFEN IN THE ORAL THERAPY OF PEYRONIE'S DISEASE: A PRELIMINARY REPORT" BJU INTERNATIONAL, BLACKWELL SCIENCE, OXFORD, GB, vol. 88, no. 1, July 2001 (2001-07), pages 63-67, XP001106370 ISSN: 1464-4096

2. The subject-matter of the present application was the use of L-acetylcarnitine in combination with L-propionylcarnitine for the treatment of disorders caused by the andropause.

3. D1 discloses pharmaceutical compositions comprising at least one compound selected from a group of compounds comprising acetylcarnitine and propionylcarnitine. The compositions are used to treat symptoms caused by Acylcarnitine Metabolic Dysfunction Syndrome (ACMDS). Among the symptoms fatigue, difficulty of thinking, inability to concentrate (aprosexia) and depression are explicitly mentioned.

   D2 discloses pharmaceutical compositions comprising at least one compound selected from a group of compounds comprising L-acetylcarnitine and L-propionylcarnitine. Among the treatable disorders osteoporosis is explicitly mentioned.

D3 and D4 disclose L-propionylcarnitine (D3) and L-acetylcarnitine (D4) for the treatment of Peyronie's disease. This indication falls within the scope of the term "reduced quality of erection" as claimed in claim 2 of the present application.

4. None of the documents D1-D4 discloses explicitly the combination of L-acetylcarnitine and L-propionylcarnitine for the treatment of the claimed diseases. It therefore appears, that present claims 1-9 fulfill the criteria of Art. 33(2) PCT.

5. As for the inventive step the following comments apply:
L-acetylcarnitine and L-propionylcarnitine are known in the art for the treatment of disorders which falls within the scope of the present application (see item 3).
It would be obvious for the skilled person to combine these compounds and doing so the skilled person would arrive at the subject-matter as claimed in the present application.
No additional surprising/unexpected effect evidenced by for example comparative data with the single compounds can be regarded from the present application.
Therefore it appears, that the subject-matter of the present application does not fulfil the criteria of Art. 33(3) PCT.